



**Common Stock**

**Pre-Funded Warrants to Purchase Common Stock**

This free writing prospectus relates only to the public offering described below and should be read together with the preliminary prospectus supplement dated December 8, 2025, or the Preliminary Prospectus Supplement, including the documents incorporated by reference therein, and the accompanying base prospectus. This free writing prospectus supplements the Preliminary Prospectus Supplement and, to the extent inconsistent, supersedes the information in the Preliminary Prospectus Supplement. This free writing prospectus supplements the Preliminary Prospectus Supplement primarily to reflect the addition of certain pre-funded warrants, and the shares of common stock issuable upon the exercise of such pre-funded warrants, to the securities being offered by Fulcrum Therapeutics, Inc. Except as otherwise indicated, all information in this free writing prospectus and the Preliminary Prospectus Supplement assumes no exercise of outstanding options or warrants, no settlement of outstanding restricted stock units, no exercise of the underwriters' option to purchase additional shares of our common stock and no exercise of the pre-funded warrants included in this offering.

This free writing prospectus is qualified in its entirety by reference to the Preliminary Prospectus Supplement, including the documents incorporated by reference therein, and the accompanying base prospectus. Financial information and other information presented in the Preliminary Prospectus Supplement or incorporated by reference therein is deemed to have changed to the extent affected by the changes described herein. This free writing prospectus should be read together with the Preliminary Prospectus Supplement, including the documents incorporated by reference therein, and the accompanying base prospectus, before making a decision in connection with an investment in the securities. Capitalized terms used in this free writing prospectus but not defined have the meanings given to them in the Preliminary Prospectus Supplement.

**Common stock offered by us**

shares of common stock

**Pre-funded warrants offered by us**

We are also offering, in lieu of common stock, pre-funded warrants to purchase up to shares of our common stock to certain investors whose purchase of shares of common stock in this offering would otherwise result in such investor, together with its affiliates, beneficially owning shares of common stock with a value of or in excess of (i) the notification threshold of the HSR Act, or (ii) 4.99% (or, at the election of the purchaser, 9.99%) of the total number of shares of our common stock outstanding immediately after giving effect to such exercise. The purchase price of each pre-funded warrant will equal the price per share at which shares of common stock are being sold to the public in this offering, minus \$0.001, which is the exercise price of each pre-funded warrant. The pre-funded warrants do not expire, and each pre-funded warrant will be exercisable at any time after

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the date of issuance, subject to an ownership limitation and in some cases clearance under the HSR Act. See “Description of Pre-Funded Warrants” in this free writing prospectus for additional information. This free writing prospectus and the Preliminary Prospectus Supplement also relates to the offering of the shares of common stock issuable upon the exercise of such pre-funded warrants.

**Option to purchase additional shares**

The underwriters have a 30-day option to purchase up to an additional \$22,500,000 of shares of common stock.

**Common stock to be outstanding immediately after this offering**

\_\_\_\_\_ shares (\_\_\_\_\_ shares if the underwriters exercise their option to purchase additional shares in full), in each case assuming no exercise of any pre-funded warrants offered and to be sold by us.

**Use of proceeds**

We estimate that the net proceeds to us from this offering will be approximately \$ \_\_\_\_\_ million, or approximately \$ \_\_\_\_\_ million if the underwriters exercise their option to purchase additional shares in full.

We currently intend to use the net proceeds from the sale of securities offered under this free writing prospectus and the Preliminary Prospectus Supplement primarily for general corporate purposes, which may include working capital and capital expenditures, research and development expenses, including to fund clinical trials, regulatory submissions, commercialization, discovery and additional preclinical research and development of additional product candidates and platform enhancement, general and administrative expenses, and potential acquisitions of, or investments in, companies, technologies, products or assets that complement our business. See “Use of Proceeds” in this free writing prospectus and the Preliminary Prospectus Supplement for more information.

**Risk factors**

You should read the “Risk Factors” in this free writing prospectus, the accompanying base prospectus, and the risks set forth under the caption “Item 1A. Risk Factors” included in our Quarterly Report on Form 10-Q for the three months ended September 30, 2025 and the other documents incorporated by reference into this free writing prospectus and the Preliminary Prospectus Supplement for a discussion of factors to consider carefully before deciding to purchase our securities.

**Nasdaq Global Market Symbol**

“FULC”. We do not intend to list the pre-funded warrants on The Nasdaq Global Market or any other national securities exchange or any recognized trading system. Without an active market, the liquidity of the pre-funded warrants will be limited.

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**Risk Factors**

*Investing in our securities involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this free writing prospectus, the Preliminary Prospectus Supplement and the accompanying base prospectus and the risk factors in our most recent Annual Report on Form 10-K, our most recent Quarterly Reports on Form 10-Q, together with other information in this free writing prospectus, the Preliminary Prospectus Supplement, the accompanying base prospectus and the information and documents incorporated by reference in this free writing prospectus, the Preliminary Prospectus Supplement and the accompanying base prospectus, and in any prospectus supplement or free writing prospectus that we authorize for use in connection with this offering. If any of the following risks actually occur, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.*

**Risks Related to This Offering**

***Sale of a substantial number of shares of our common stock, including by us, could cause the market price of our common stock to drop significantly, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. All of our outstanding shares of common stock are, and the shares of common stock (including shares of common stock underlying the pre-funded warrants) sold in this offering will be, freely tradeable without restriction or further registration under the Securities Act, unless owned or purchased by our “affiliates” as that term is defined in Rule 144 under the Securities Act.

In addition, we have filed or intend to file registration statements registering all shares of common stock that we may issue under our equity compensation plans or pursuant to equity awards made to newly hired employees outside of equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

***Our management may invest or spend the proceeds of this offering in ways with which you may not agree or in ways that may not yield a return.***

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

In addition, the issuance from time to time of shares of our common stock in this offering (including shares of common stock underlying the pre-funded warrants), or our ability to issue these shares of common stock, could result in resales of our common stock by our current stockholders concerned about the potential dilution of their holdings. In turn, these resales could have the effect of depressing the market price for our common stock.

***Purchasers will experience immediate dilution in the book value per share of the common stock purchased in the offering.***

The price of the securities to be sold in this offering is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock (or pre-funded warrants in lieu thereof) in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. After giving effect to the sale of shares of our common stock and pre-funded warrants in the aggregate amount of \$ [redacted] at the public offering price of \$ [redacted] per share of common stock and \$ [redacted] per pre-funded warrant, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2025 would have been approximately \$ [redacted] million, or approximately \$ [redacted] per share. This represents an immediate increase in as adjusted net tangible book value of approximately \$ [redacted] per share to our existing stockholders and an immediate dilution in as adjusted net tangible book value of approximately \$ [redacted] per share to purchasers of our common stock or pre-funded warrants in this offering. See “Dilution” in this free writing prospectus and the Preliminary Prospectus Supplement for more information.

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***The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.***

The trading price of our common stock has been, and is likely to continue to be, volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. During the period from July 18, 2019 to December 8, 2025, the closing price of our common stock ranged from a high of \$30.97 per share to a low of \$2.26 per share. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies.

***You may experience future dilution as a result of future equity offerings.***

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by any investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by any investors in this offering.

***We do not anticipate paying any cash dividends on our common stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.***

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

***There is no public market for the pre-funded warrants being offered in this offering.***

There is no public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to list the pre-funded warrants on The Nasdaq Global Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited.

***Except for the right to participate in certain dividends and distributions, holders of the pre-funded warrants will have no rights as common stockholders until such holders exercise their pre-funded warrants and acquire our common stock.***

Until holders of the pre-funded warrants exercise their pre-funded warrants and acquire shares of our common stock, such holders will have no rights with respect to the shares of our common stock underlying such pre-funded warrants, except that the holder of a pre-funded warrant shall be entitled to participate in certain distributions, including cash dividends, if any, to all holders of our common stock for no consideration, subject to certain ownership limitations and in some cases clearance under the HSR Act. Upon exercise of the pre-funded warrants, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

***Significant holders or beneficial owners of our common stock may not be permitted to exercise the pre-funded warrants that they hold.***

A holder of the pre-funded warrants will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock beneficially owned by such holder (together with its affiliates) to exceed 4.99% (or, at the election of the purchaser, 9.99%) of the number of shares of our common stock outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 4.99% (or, at the election of the purchaser, 9.99%) of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants and subject to such holder's rights under the pre-funded warrants to increase or decrease such

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percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. In addition, where a holder notifies us that a filing under the HSR Act is required, we may not effect the exercise of any portion of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant, which, upon giving effect to such exercise, would cause the aggregate number of shares of our common stock beneficially owned by the holder (together with its attribution parties) to equal or exceed the HSR Threshold (as defined below), until the applicable waiting period under the HSR Act has expired. As a result, you may not be able to exercise your pre-funded warrants for shares of our common stock at a time when it would be financially beneficial for you to do so. In such a circumstance, you could seek to sell your pre-funded warrants to realize value, but you may be unable to do so in the absence of an established trading market.

***We will not receive any meaningful amount of additional funds upon the exercise of the pre-funded warrants.***

Each pre-funded warrant will be exercisable until it is fully exercised and by means of payment of the nominal cash purchase price upon exercise or by means of a "cashless exercise" according to a formula set forth in the pre-funded warrant. Accordingly, we will not receive any meaningful additional funds upon the exercise of the pre-funded warrants.

#### **Use of Proceeds**

We estimate that the net proceeds to us from the issuance and sale of \_\_\_\_\_ shares of common stock (or pre-funded warrants in lieu thereof) in this offering will be approximately \$ \_\_\_\_\_ million, or approximately \$ \_\_\_\_\_ million if the underwriters exercise their option to purchase additional shares in full, in each case after deducting underwriting discounts and commissions and estimated offering expenses payable to us. We will receive nominal proceeds, if any, from any exercise of pre-funded warrants.

We currently anticipate that we will use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, primarily for general corporate purposes, which may include working capital and capital expenditures, research and development expenses, including to fund clinical trials, regulatory submissions, commercialization, discovery and additional preclinical research and development of additional product candidates and platform enhancement, general and administrative expenses, and potential acquisitions of, or investments in, companies, technologies, products or assets that complement our business.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual use of the net proceeds may vary significantly depending on numerous factors, including the actual net proceeds from this offering, the progress of our development, the status of and results from clinical trials, the timing of regulatory submissions and the outcome of regulatory review, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending the use of proceeds described above, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

#### **Dilution**

If you invest in our common stock, or pre-funded warrants in lieu thereof, in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock or pre-funded warrants you will pay in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value as of September 30, 2025 was approximately \$198.4 million, or \$3.67 per share of our common stock. Our historical net tangible book value is the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share represents historical net tangible book value divided by the 54,108,438 shares of our common stock outstanding as of September 30, 2025.

After giving effect to the issuance and sale of \_\_\_\_\_ shares of our common stock that we are offering at the public offering price of \$ \_\_\_\_\_ per share, and pre-funded warrants to purchase up to \_\_\_\_\_ shares of common stock at the public offering price of \$ \_\_\_\_\_ per pre-funded warrant (which equals the public offering price of the common stock at which shares of our common stock are being sold to the public in this offering less the \$0.001 per share exercise price of each such pre-funded warrant) (excluding shares of common stock issuable upon exercise of the pre-funded warrants, any proceeds which may be received upon exercise of the pre-funded warrants or any resulting accounting associated with the exercise of the pre-funded warrants), and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value at September 30, 2025 would have been approximately \$ \_\_\_\_\_ million, or \$ \_\_\_\_\_ per share. This represents an immediate increase in as adjusted net tangible book value of \$ \_\_\_\_\_ per share to existing stockholders and an immediate dilution of \$ \_\_\_\_\_ per share to investors in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this per share dilution.

Public offering price per share	\$
Historical net tangible book value per share as of September 30, 2025	\$3.67
Increase in net tangible book value per share attributable to this offering	
As adjusted net tangible book value per share after giving effect to this offering	
Dilution per share to new investors purchasing shares in this offering	<u>\$</u>

Assuming the pre-funded warrants were immediately and fully exercised, this would result in an as adjusted net tangible book value per share, after giving effect to this offering and pre-funded warrant exercise, of \$ \_\_\_\_\_, or \$ \_\_\_\_\_ per share. This represents an increase in net tangible book value of \$ \_\_\_\_\_ per share to existing stockholders and dilution in net tangible book value per share of \$ \_\_\_\_\_ to new investors participating in this offering.

If the underwriters exercise their option to purchase additional shares in full, the immediate dilution in as adjusted net tangible book value per share to investors in this offering would be \$ \_\_\_\_\_ per share.

The table and discussion above are based on 54,108,438 shares of our common stock outstanding as of September 30, 2025, and exclude the following:

- 11,870,785 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2025 at a weighted average exercise price of \$6.57 per share;
- 69,486 shares of common stock issuable upon vesting of RSUs outstanding as of September 30, 2025;
- 4,779,386, 1,681,184 and 2,052,030 shares of our common stock available for future issuance as of September 30, 2025 under the 2019 Plan, the Inducement Plan and the ESPP, respectively, as well as any automatic increases in the number of shares of common stock reserved under these plans; and
- 8,500,000 shares of common stock issuable upon the exercise of pre-funded warrants outstanding as of September 30, 2025 at an exercise price of \$0.001 per share.

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Further, the number of shares of our common stock to be outstanding after this offering does not take into account the \_\_\_\_\_ shares of our common stock issuable upon the exercise of the pre-funded warrants.

To the extent that outstanding stock options are exercised, outstanding RSUs are settled, outstanding or new pre-funded warrants are exercised, new stock options are issued, or we issue additional shares of common stock in the future, including pursuant to our Controlled Equity Offering<sup>SM</sup> Agreement with Cantor Fitzgerald & Co. and Stifel, Nicolas & Company, Incorporated, there will be further dilution to investors purchasing securities in this offering.

### **Description of Pre-Funded Warrants**

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

#### **Form**

The pre-funded warrants will be issued as individual warrant agreements to investors. The form of pre-funded warrant will be filed as an exhibit to a Current Report on Form 8-K that we expect to file with the SEC.

#### **Term**

The pre-funded warrants do not expire.

#### **Exercisability**

The pre-funded warrants are exercisable at any time on or after their original issuance. The pre-funded warrants are exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the fair market value of the common stock on the exercise date.

#### **Exercise Limitations**

We may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause the aggregate number of shares of our common stock beneficially owned by the holder (together with its attribution affiliates (as defined below)) to exceed 4.99% (or, at the election of the purchaser, 9.99%) of the number of shares of our common stock that would be outstanding immediately after giving effect to the exercise. However, any holder of a pre-funded warrant may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. For purposes of the foregoing, "attribution affiliates" means, collectively, the following persons and entities with respect to any holder: (i) its direct or indirect affiliates, (ii) any person acting or who could be deemed to be acting as a Section 13(d) "group" together with the holder or any attribution parties and (iii) any other persons whose beneficial ownership of our common stock would or could be aggregated with the holder and/or any other attribution parties for purposes of Section 13(d) or Section 16 of the Exchange Act.

In addition, if the exercise of a pre-funded warrant would result in a holder of pre-funded warrants (together with its attribution affiliates) acquiring beneficial ownership of our common stock (together with all other equity owned by such holder at such time) equal to or in excess of the notification threshold applicable to the holder under the HSR Act as of the date of delivery of the applicable exercise notice, which we refer to as the HSR Threshold, and no exemption to filing a notice and report form under the HSR Act is applicable, then only such portion of the pre-funded warrants held by such holder, which when exercised does not exceed the HSR Threshold, shall be exercisable and the applicable exercise notice shall be deemed to relate only to such portion of the pre-funded warrants, and the remaining portion of the pre-funded warrants in excess of the HSR Threshold shall not be exercisable until the expiration or early termination of the applicable waiting period under the HSR Act or receipt of applicable approval.

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**Exercise Price**

The exercise price per whole share of our common stock purchasable upon the exercise of the pre-funded warrants is \$0.001 per share of common stock. The exercise price of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distributions of assets, including cash, stock or other property to our stockholders.

**Transferability**

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent. The ownership of the pre-funded warrants and any transfers of the pre-funded warrants will be registered in a warrant register maintained by the warrant agent. We will initially act as warrant agent.

**Exchange Listing**

There is no established trading market for the pre-funded warrants, and we do not expect a market to develop. We do not plan on applying to list the pre-funded warrants on The Nasdaq Global Market or any other national securities exchange or any nationally recognized trading system.

**Fundamental Transactions**

In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercise contained in the pre-funded warrants. In the event a holder does not exercise its pre-funded warrants in connection with a fundamental transaction, such holder's pre-funded warrants will be deemed exercised in full pursuant to the "cashless exercise" mechanic described above upon the consummation of such transaction.

**Rights as a Stockholder**

Except by virtue of such holder's ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the pre-funded warrant. In the event of certain distributions, including cash dividends, if any, to all holders of our common stock for no consideration, the holder of a pre-funded warrant shall be entitled to participate in such distributions to the same extent as if such holder held the number of shares of our common stock acquirable upon complete exercise of its pre-funded warrant (without regard to any limitations on exercise). If such distribution would result in such holder and its affiliates to exceed the exercise limitations described above, a portion of such distribution shall be held in abeyance for the benefit of such holder until such time as the ownership limitations would not be exceeded.

**MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR INVESTORS IN COMMON STOCK AND PRE-FUNDED WARRANTS**

The following summary describes the material U.S. federal income tax considerations applicable to the acquisition, ownership and disposition of our common stock and pre-funded warrants acquired in this offering. This discussion does not address all aspects of U.S. federal income taxes, does not discuss the potential application of the alternative minimum tax or Medicare Contribution tax and does not deal with state or local taxes, U.S. federal gift and estate tax laws or any non-U.S. tax consequences that may be relevant to investors in light of their particular circumstances.

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Special rules different from those described below may apply to certain investors that are subject to special treatment under the Internal Revenue Code of 1986, as amended, or the Code, such as:

- insurance companies, banks and other financial institutions;
- tax-exempt organizations (including private foundations) and tax-qualified retirement plans;
- foreign governments and international organizations;
- broker-dealers and traders in securities;
- U.S. expatriates and former citizens or long-term residents of the United States;
- Non-U.S. Holders (as defined below) that own, or are deemed to own, more than 5% of our common stock (directly, indirectly or by attribution) or more than 5% of our pre-funded warrants;
- persons required for U.S. federal income tax purposes to conform the timing of income accruals to their financial statements under Section 451(b) of the Code;
- “controlled foreign corporations,” “passive foreign investment companies” and corporations that accumulate earnings to avoid U.S. federal income tax;
- persons that hold our common stock or pre-funded warrants as part of a “straddle,” “hedge,” “conversion transaction,” “synthetic security” or integrated investment or other risk reduction strategy;
- U.S. Holders (as defined below) whose functional currency for U.S. tax purposes is not the U.S. dollar;
- persons who do not hold our common stock or pre-funded warrants as “capital assets” within the meaning of Section 1221 of the Code (generally, for investment purposes); and
- partnerships and other pass-through entities, and investors in such pass-through entities (regardless of their places of organization or formation).

Such investors are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them.

Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, possibly retroactively, and are subject to differing interpretations which could result in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the Internal Revenue Service, or the IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions or will not take a contrary position regarding the tax consequences described herein, or that any such contrary position would not be sustained by a court.

For the purposes of this discussion, a “U.S. Holder” means a beneficial owner of our common stock or pre-funded warrants, other than a partnership or other pass-through entity, that is, for U.S. federal income tax purposes, (a) an individual citizen or resident of the United States, (b) a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes), created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is subject to U.S. federal income taxation regardless of its source, or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more “United States persons” (within the meaning of Section 7701(a)(30) of the Code) have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a United States person.

If you are an individual non-U.S. citizen, you may, in some cases, be deemed to be a resident alien (as opposed to a nonresident alien) by virtue of being present in the United States for at least 31 days in the calendar year and for an aggregate of at least 183 days during a three-year period ending in the current calendar year. Generally, for this purpose, all the days present in the current year, one-third of the days present in the immediately preceding year, and one-sixth of the days present in the second preceding year, are counted.

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Resident aliens are generally subject to U.S. federal income tax as if they were U.S. citizens. Individuals who are uncertain of their status as resident or nonresident aliens for U.S. federal income tax purposes are urged to consult their own tax advisors regarding the U.S. federal income tax consequences of the ownership or disposition of our common stock or pre-funded warrants.

PERSONS CONSIDERING THE PURCHASE OF OUR COMMON STOCK OR PRE-FUNDED WARRANTS PURSUANT TO THIS OFFERING SHOULD CONSULT THEIR OWN TAX ADVISORS CONCERNING THE U.S. FEDERAL INCOME TAX CONSEQUENCES OF ACQUIRING, OWNING AND DISPOSING OF OUR COMMON STOCK AND PRE-FUNDED WARRANTS IN LIGHT OF THEIR PARTICULAR SITUATIONS AS WELL AS ANY CONSEQUENCES ARISING UNDER THE LAWS OF ANY OTHER TAXING JURISDICTION, INCLUDING ANY STATE, LOCAL OR NON-U.S. TAX CONSEQUENCES OR ANY U.S. FEDERAL NON-INCOME TAX CONSEQUENCES, AND THE POSSIBLE APPLICATION OF TAX TREATIES.

#### **Characterization of the Pre-Funded Warrants for Tax Purposes**

Although the characterization of the pre-funded warrants for U.S. federal income tax purposes is not entirely clear, because the exercise price of the pre-funded warrants is a nominal amount, we expect to treat the pre-funded warrants as our common stock for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of common stock as described below. Accordingly, for U.S. federal income tax purposes, no gain or loss should be recognized upon the exercise of a pre-funded warrant, and upon exercise, the holding period of the share of common stock received should include the holding period of the pre-funded warrant. Similarly, the tax basis of a share of common stock received upon exercise of a pre-funded warrant should include the tax basis of the pre-funded warrant increased by the exercise price of \$0.001 per share. The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes.

Our position with respect to the characterization of pre-funded warrants is not binding on the IRS and the IRS may treat the pre-funded warrants as warrants to acquire our common stock and, if so, the amount and character of your gain with respect to an investment in our pre-funded warrants could change. You should consult your tax advisor regarding the characterization of pre-funded warrants for U.S. federal income tax purposes, and the consequences to you of an investment in the pre-funded warrants based on your own particular facts and circumstances.

#### **Tax Consequences to U.S. Holders**

##### ***Distributions on Common Stock and Pre-funded Warrants***

We do not expect to make distributions on our common stock (or pre-funded warrants) in the foreseeable future. In the event that we do make distributions of cash or other property, distributions paid on common stock (or pre-funded warrants) will be treated as a dividend to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles), and will be includible in your income as ordinary income when received. However, with respect to dividends received by individuals, such dividends are generally taxed at the lower applicable long-term capital gains rates, provided certain holding period requirements are satisfied. Distributions in excess of our current and accumulated earnings and profits will be treated as a return of capital to the extent of a U.S. Holder's tax basis in the common stock (or pre-funded warrant) and thereafter as capital gain from the sale or exchange of such common stock (or pre-funded warrant). The tax treatment of such gain is further described in "—Sale or Other Disposition of Common Stock or Pre-Funded Warrants" below. Dividends received by a corporation may be eligible for a dividends received deduction, subject to applicable limitations. Any such distributions will also be subject to the discussions below under the section titled "—Information Reporting and Backup Withholding."

A U.S. Holder of a pre-funded warrant is expected to receive any distributions paid with respect to common stock prior to the exercise of the pre-funded warrant and, in such case, would be taxed in the same manner as a U.S. Holder of common stock that receives such a distribution. However, under certain circumstances, it is possible for cash to be held in abeyance for the U.S. Holder until a pre-funded warrant is exercised or the ownership limitations (described under "Description of Pre-Funded Warrants") would not be exceeded, at which time such U.S. Holder shall be entitled to receive distributions. It is possible that such entitlement to distributions could cause the declaration of a distribution on our common stock to be currently taxable to U.S. Holders of pre-funded warrants, including under the principles governing Section 305 of the Code, even though the holders will not receive such

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distributions until a future date. Additionally, it is possible that other adjustments to the terms of the pre-funded warrant may be considered constructive distributions under Section 305 of the Code and taxable as discussed above. A holder of a pre-funded warrant should consult its tax advisor regarding the tax treatment of any distribution with respect to such pre-funded warrant that is held in abeyance in connection with any applicable limitation on the holder's beneficial ownership of our common stock.

#### ***Sale or Other Disposition of Common Stock or Pre-Funded Warrants***

For U.S. federal income tax purposes, gain or loss realized on the sale or other disposition of common stock or pre-funded warrants will be capital gain or loss, and will be long-term capital gain or loss if you have held the common stock or pre-funded warrants for more than one year. The amount of the gain or loss will equal the difference between your tax basis in the common stock or pre-funded warrants disposed of and the amount realized on the disposition. Long-term capital gains recognized by non-corporate U.S. Holders will be subject to reduced tax rates. The deductibility of capital losses is subject to limitations.

#### ***Information Reporting and Backup Withholding***

Information reporting requirements generally will apply to any payments of dividends on our common stock and pre-funded warrants, constructive dividends on our pre-funded warrants, and gross proceeds on the sale or other disposition of our common stock and pre-funded warrants, unless the U.S. Holder is an exempt recipient (such as a corporation). Backup withholding (currently at a 24% rate) will apply to those payments if the U.S. Holder fails to provide its correct taxpayer identification number, or certification of exempt status, or if the U.S. Holder is notified by the IRS that it has failed to report in full payments of interest and dividend income. Any amounts withheld under the backup withholding rules will be allowed as a refund or a credit against a U.S. Holder's U.S. federal income tax liability provided the required information is furnished timely to the IRS.

#### ***Tax Consequences to Non-U.S. Holders***

For purposes of this discussion, a Non-U.S. Holder is a beneficial owner of our common stock or pre-funded warrants, other than a partnership or other pass-through entity that is (i) a non-resident alien individual, (ii) a corporation or other foreign organization taxable as a corporation for U.S. federal income tax purposes that is created or organized in or under laws other than the laws of the United States, any state thereof, or the District of Columbia; (iii) an estate, the income of which is not subject to U.S. federal income tax on a net income basis; or (iv) a trust the income of which is not subject to U.S. federal income tax on a net income basis and that (1) has not made an election to be treated as a U.S. person under applicable U.S. Treasury Regulations and (2) either (i) is not subject to the primary supervision of a court within the United States or (ii) is not subject to the substantial control of one or more U.S. persons is not a U.S. Holder. If you are not a Non-U.S. Holder, this section does not apply to you.

#### ***Distributions on Common Stock and Pre-funded Warrants***

We do not expect to make any distributions on our common stock (or pre-funded warrants) in the foreseeable future. If we do make distributions on our common stock (or pre-funded warrants), however, such distributions made to a Non-U.S. Holder will constitute dividends for U.S. tax purposes to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Distributions in excess of our current and accumulated earnings and profits will constitute a return of capital that is applied against and reduces, but not below zero, a Non-U.S. Holder's adjusted tax basis in our common stock (or pre-funded warrants). Any remaining excess will be treated as gain realized as described below under the section titled "—Sale or Other Disposition of Common Stock and Pre-Funded Warrants."

Any distribution on our common stock (or pre-funded warrants) that is treated as a dividend paid to a Non-U.S. Holder that is not effectively connected with the holder's conduct of a trade or business in the United States will generally be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and the Non-U.S. Holder's country of residence. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide the applicable withholding agent with a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E or other appropriate form, certifying the Non-U.S. Holder's entitlement to benefits under that treaty. Such form must be provided prior to the payment of dividends and must be updated periodically. If a Non-U.S. Holder holds stock through a financial institution or other agent acting

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on the holder's behalf, the holder will be required to provide appropriate documentation to such agent. The holder's agent may then be required to provide certification to the applicable withholding agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. withholding tax under an income tax treaty, you should consult with your own tax advisor to determine if you are able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

We generally are not required to withhold tax on dividends paid (or constructive dividends deemed paid) to a Non-U.S. Holder that are effectively connected with the holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that the holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if shares of our common stock are held through a financial institution or other agent, to the applicable withholding agent). In general, such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates applicable to U.S. persons, unless a specific treaty exemption applies. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional "branch profits tax," which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder's effectively connected earnings and profits, subject to certain adjustments.

A Non-U.S. Holder of a pre-funded warrant is expected to receive any distributions paid with respect to common stock prior to the exercise of the pre-funded warrant and, in such case, would be taxed in the same manner as a Non-U.S. Holder of common stock that receives such a distribution. However, under certain circumstances, it is possible for cash to be held in abeyance for a Non-U.S. Holder until a pre-funded warrant is exercised or the ownership limitations (described under "Description of Pre-Funded Warrants") would not be exceeded, at which time the Non-U.S. Holder shall be entitled to receive distributions. It is possible that such entitlement to distributions could cause the declaration of a distribution on our common stock to be currently taxable to Non-U.S. Holders of pre-funded warrants, including under the principles governing Section 305 of the Code, even though such holders will not receive the distributions until a future date. Additionally, it is possible that other adjustments to the terms of the pre-funded warrant may be considered constructive distributions under Section 305 of the Code and taxable as discussed above. A holder of a pre-funded warrant should consult its tax advisor regarding the tax treatment of any distribution with respect to such pre-funded warrant that is held in abeyance in connection with any applicable limitation on the holder's beneficial ownership of our common stock.

See also the section below titled "—Foreign Accounts" for additional withholding rules that may apply to dividends paid to certain foreign financial institutions or non-financial foreign entities.

#### ***Sale or Other Disposition of Common Stock and Pre-Funded Warrants***

Subject to the discussion below under the sections titled "—Information Reporting and Backup Withholding" and "—Foreign Accounts," a Non-U.S. Holder generally will not be subject to U.S. federal income or withholding tax with respect to gain realized on a sale or other disposition of our common stock or pre-funded warrants unless (a) the gain is effectively connected with a trade or business of the holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that the holder maintains in the United States), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for a period or periods aggregating 183 or more days in the taxable year of the disposition and certain other conditions are met, or (c) we are or have been a "United States real property holding corporation" within the meaning of Code Section 897(c)(2), unless any class of our stock is regularly traded on an established securities market and the Non-U.S. Holder disposes of such class of stock and holds no more than 5% of such class of stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the Non-U.S. Holder held such class of stock.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at the regular graduated U.S. federal income tax rates applicable to U.S. persons, unless a specific treaty exemption applies. Corporate Non-U.S. Holders described in (a) above may also be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by certain U.S. source capital losses (even though you are not considered a resident of the United States), provided you have timely filed U.S. federal income tax returns with respect to such losses. With respect to (c) above, in

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general, we would be a U.S. real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our worldwide real property interests plus our other assets used or held for use in a trade or business. We believe that we are not, and do not anticipate becoming, a U.S. real property holding corporation. However, there can be no assurance that we will not become a U.S. real property holding corporation in the future.

### ***Information Reporting and Backup Withholding***

Generally, we or certain financial middlemen must report information to the IRS with respect to any dividends we pay on our common stock or pre-funded warrants and any constructive dividends deemed paid on pre-funded warrants including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient's country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E, as applicable, or otherwise establishes an exemption, provided that the applicable withholding agent does not have actual knowledge or reason to know the holder is a U.S. person.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock or pre-funded warrants effected by or through a U.S. office of any broker, U.S. or non-U.S., unless the Non-U.S. Holder provides a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E, as applicable, or otherwise meets documentary evidence requirements for establishing non-U.S. person status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Backup withholding is not an additional tax. If backup withholding is applied to you, you should consult with your own tax advisor to determine whether you have overpaid your U.S. federal income tax, and whether you are able to obtain a tax refund or credit of the overpaid amount.

### **Foreign Accounts**

In addition to, and separately from the withholding rules described above, U.S. federal withholding taxes may apply under the Foreign Account Tax Compliance Act, or FATCA, on certain types of payments, including dividends to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends paid in respect of our common stock or pre-funded warrants, constructive distributions deemed paid with respect to pre-funded warrants and the gross proceeds of the disposition on our common stock or pre-funded warrants paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution agrees to undertake certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. The 30% federal withholding tax described in this paragraph cannot be reduced under an income tax treaty with the United States. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

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The Treasury Secretary has issued proposed regulations providing that the withholding provisions under FATCA do not apply with respect to payment of gross proceeds from a sale or other disposition of our common stock or pre-funded warrants, which may be relied upon by taxpayers until final regulations are issued. Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock or pre-funded warrants.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK AND PRE-FUNDED WARRANTS, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW, AS WELL AS TAX CONSEQUENCES ARISING UNDER ANY STATE, LOCAL, NON-U.S. OR U.S. FEDERAL NON-INCOME TAX LAWS SUCH AS ESTATE AND GIFT TAX.

#### **Underwriting**

The underwriters will purchase the pre-funded warrants pursuant to the underwriting agreement described in the Preliminary Prospectus Supplement on terms generally consistent with those applicable to the shares of common stock being sold in the offering. The underwriting discounts and commissions per pre-funded warrant will be equal to the underwriting discounts and commissions per share of common stock sold in the offering. The underwriters have not been engaged to act as warrant agent for the pre-funded warrants or to act as underwriter or agent or otherwise participate in the issuance of the shares of our common stock upon the exercise of the pre-funded warrants.

#### **General**

Additional conforming changes are hereby made to the Preliminary Prospectus Supplement to reflect the changes described in this free writing prospectus. All terms of the Preliminary Prospectus Supplement applicable to our common stock will be applicable to the shares underlying the pre-funded warrants upon issuance.

**Fulcrum Therapeutics, Inc. has filed a registration statement (including a preliminary prospectus supplement dated December 8, 2025 and the accompanying base prospectus) with the SEC for the offering to which this communication relates. Before you invest, you should read the preliminary prospectus supplement and the accompanying base prospectus and other documents the Issuer has filed with the SEC for more complete information about the Issuer and the offering. You may obtain these documents for free by visiting EDGAR on the SEC website at [www.sec.gov](http://www.sec.gov). Alternatively, copies may be obtained from: J.P. Morgan Securities LLC, c/o Broadridge Financial Solutions, 1155 Long Island Avenue, Edgewood, NY 11717, or by email at [prospectus-eq\\_fi@jpmorgan.com](mailto:prospectus-eq_fi@jpmorgan.com) and [postsalemanualrequests@broadridge.com](mailto:postsalemanualrequests@broadridge.com); Leerink Partners LLC, Attention: Syndicate Department, 53 State Street, 40th Floor, Boston, MA 02109, by telephone at (800) 808-7525, ext. 6105, or by email at [syndicate@leerink.com](mailto:syndicate@leerink.com); Cantor Fitzgerald & Co. by mail at Attention: Capital Markets, 110 East 59th Street, New York 10022 or by email at [prospectus@cantor.com](mailto:prospectus@cantor.com); Oppenheimer & Co. Inc. Attention: Syndicate Prospectus Department, 85 Broad Street, 26th Floor, New York, NY 10004, or by telephone at (212) 667-8055, or by email at [EquityProspectus@opco.com](mailto:EquityProspectus@opco.com); or Truist Securities, Inc., Attention: Equity Capital Markets, 740 Battery Ave SE, Atlanta, Georgia 30339, by telephone at (800) 685-4786 or by email at [truistsecurities.prospectus@truist.com](mailto:truistsecurities.prospectus@truist.com).**

